UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/402,446	01/18/00	PRICE	H	7841-89

001059 HM12/0509
BERESKIN AND PARR
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AIR MAIL

EXAMINER	
HINES, J	
ART UNIT	**PAPER NUMBER**
1645	7

DATE MAILED: 05/09/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/402,446	PRICE ET AL.	
	Examiner	Art Unit	
	Ja-Na A Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-22 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-22 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Claim Objections

1. Claim 26 is objected to because of the following informalities: Claim 26 is drawn to claim 23 however there is no claim, 23. Furthermore, there are no claims 23-25, thus there should be no claim 26. Therefore, appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-22 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear how to define "increase the serum life." Neither the specification nor the claims define what level of increase is required. Further, it is unclear what the increase in serum life is being compared to in order to determine whether there has been an increase. It is unclear if the increase is compared to immune globulin without a nonionic surfactant or compared to a specific nonionic surfactant. Therefore, the claims are vague and indefinite.

3. Claims 19 and 21 are vague and indefinite. It is unclear how to define "to reduce the elevation of neutrophil counts." The phrase is vague and indefinite because it is unclear how to define a reduction of elevation of neutrophils. How much reduction in the elevation is required? Neither the specification nor the claims define how much of a reduction in elevation is needed. Therefore, the claims are indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 7, 9-12, 14-15, 18 and 20, are rejected under 35 U.S.C. 102(b) as being anticipated by Beggs et al. (WO 95/01155). Beggs et al., (WO 95/01155) a comprising an antibody and a surfactant. The class of nonionic surfactant combines good compatibility with the antibodies, providing improved immunoreactivity on longer term storage and enhancing antibody binding and/or enzyme activity (pages 1-2 lines 36-3). The surfactant comprises a nonionic surfactant (page 2 lines 5-7). The nonionic surfactant acts as a stabilizing agent in an antibody-containing composition (page 2 lines 10-12). An essential element in the nonionic surfactant is basically the condensation product of alkylene oxides with a hydrophobic moiety (page 2 lines 13-16). Typical examples of such products include ethylene oxide, propylene oxide and further suitable examples can be found in such sources such as "Nonionic Surfactants" (page 2 lines 25-28). Another type of preferred nonionic surfactant is the class of alkoxylated fatty acid esters (page 3 lines 8-10). Other suitable examples included polyoxyethylene sorbitan, monolaurate and polyoxyethylene sorbitan monooleate known as TWEEN 20 and TWEEN 80 which are commercially available (page 3 lines 14-18). Mixtures of various nonionic surfactant may also be used (page 3 lines 19). The nonionic surfactants were used in an amo8unt of 0.01-6%, usually 0.1-3% and

preferably 0.25-2% by weight (page 3 lines 19-21). An effective amount of the antibody was used (page 3 lines 33-34). Wherein antibodies include polyclonal and monoclonal antibodies, as well as fragments (page 1 lines 19-24). Such compositions can be in aqueous solutions (page 6 lines 9-11). Example 5 teaches the stability of antibodies with a variety of ingredients.

Therefore, Beggs et al., teaches the invention as claimed.

5. Claims 1, 7, 9-12, 14-15, 17-20 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Hirao et al., (EP 278,422). Hirao et al., (EP 278,422) teaches a solution of chemically unmodified complete molecular type γ-globulin that can be administered intravenously (page 2 lines 4-5). The injectable solution comprising sorbitan as a stabilizer has a low electrical conductivity which does not cause an increase of γ-globulin polymer, a rise of anticomplement titer, or impairment of the activities of the γ-globulin, either during preservation or upon administration to a living body (page 2 lines 30-36). γ-globulin is treated in the presence of stabilizer and can be in a dissolved state in the form of an aqueous solution (page 5 lines 20-23). The stabilizer can be either dry or wet treatment and preferably includes disaccharides and sugar alcohols such as sorbitol or mannitol (page 5 lines 23-26). The recommended amount of stabilizer is from 0.5 to 5w/v% (page 5 lines 25-27). This procedure allows the stability of the immunoglobulin during the heating to be ensured by conducting the heat treatment in an inert gas atmosphere (page 5 lines 31-39). Preparation and purification of the γ-globulin to be used can be achieved by methods known in the art

including wet heat treatment, PEG treatment, blood-group substance treatment and anion exchange treatment (page 5 lines 42-45). Test example 1 teaches a liquid composition wherein each stabilizer was tested. See Table 1.

Therefore Hirao et al., teaches the invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 2-4, 8, 15-17, 19-20, 22 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beggs et al. (WO 95/01155) in view of Friesen (CA 1,168,152). Beggs et al. (WO 95/01155).has been discussed above, however it does not teach the use of the anti-Rh_oD immune globulin. Friesen (CA 1,168,152) teaches manufacturing of human plasma fractions contained immune globulin (IgG) where in such fractions may be obtained in concentrated aqueous solution and are useful for intravenous injection (page 1 lines 1-5). The dilute solution containing the IgG is treated with a mixture of sodium chloride and glycine and the dilute solution thus obtained is subject to ultrafiltration to provide a concentrated solution containing IgG. The concentration of the glycine is 0.1M and the sodium chloride is 0.15M. (page 3 lines 23-27). The solution may be freeze-dried to provide a solid composition. The process is suitable for preparing Rh immune globulin for the prevention of Rh isoimmunization by passive

administration of anti-D (page 1 lines 18-21). Intravenous injection results in a much more rapid appearance of the Rh antibody in the circulation as well as a higher maximum level and such injection cause less discomfort then the intramuscular route (page 2 lines 1-4). The purity, anticomplementary activity, safety and other test results were determined according to established procedures before the product (WINRHO) was used in clinical trials (page 4 lines 24-30). The WinRho product is also known as the anti-Rh_oD immune globulin. The authors teach the preparation of Rh immune globulin (pages 4-5 lines 30- 21). The purity and recovery of IgG depends upon the ionic strength and pH of eluting buffer, wherein high-purity occur (page 9 lines 7-13). The ultrafiltration process concentrates the dilute solution from about 1/10 to about 1-100 of the volume of said dilute solution.

Therefore, no more then routine skill would have been required at the time of applicants invention to use the known and commercially available anti-Rh_oD immune globulin as taught by Friesen with the well known serum-life enhancing stabilizers of Beggs et al., because Friesen teaches that the anti-Rh_oD immune globulin can be intravenously administered to patients to prevent Rh isoimmunization.

7. Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beggs et al. (WO 95/01155) in view of Moore et al. Beggs et al. (WO 95/01155).has been discussed above, however it does not teach the use of the anti-c immune globulin. Moore et al., teaches antibody detection. Samples were found to contain anti-c

antibody (page 383). The optical density reading also detected the anti-c antibody (page 383). Tables 1 shows that a comparison of sensitivity of manual and automated tests detecting anti-c. Table 2 results testing antisera, diluted 1:4 in the autoanalyzer.

Therefore, no more then routine skill would have been required at the time of applicants invention to use the known anti-c immune globulin as taught by Moore et al., with the well known serum-life enhancing stabilizers of Beggs et al., because Moore et al., teaches that the anti-c immune globulin already detectable and known to be found in human sera.

8. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Beggs et al. (WO 95/01155) in view of Jansen et al., (EP 318,081). Beggs et al. (WO 95/01155).has been discussed above, however it does not teach the use two or more non-ionic surfactants. Jansen et al., (EP 318,081) teaches the stabilization of antibodies. In aqueous solutions of antibodies are physically stable for a sufficiently long time if they also contain a combination of a polyoxypropylene-polyoxyethylene block polymer (POP-POE block polymer) and a phospholipid (page 2 lines 17-19). No aggregation of the antibodies occurs and the composition solution remains clear and homogeneous while the activity of the peptide also remains intact (page 2 lines 20-23). The stabilized antibodies may be from antiserum or produced from immortalized B-lymphocytes or other known ways to produce antibodies (page 3 lines 15-20). Examples 1 and 2 teach the use of glycine and benzyl alcohol in the composition. Furthermore, the stability and activity of the antibody solutions described in examples 1

and 2 have been studied for many months and were also compared to compositions with no POP-POE block polymer. See the Table on page 6.

Accordingly, no more then routine skill would have been required at the time of applicants invention to use two or more non-ionic surfactants as taught by Jansen et al., with the well known serum-life enhancing stabilizers of Beggs et al., who also teaches that mixtures of non-ionic surfactants is known in the art, because Jansen et al., teaches that aqueous solutions of antibodies are physically more stable for long periods of time if they contain a combination of a polyoxypropylene-polyoxyethylene surfactants.

Prior Art

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Alonso (EP 764,447) teaches intravenously injectable immune serum globulin. Eibl et al., (US Patent 4,276,283) teaches methods for preparing an intravenously administratrable immune globulin preparation containing antibodies and preparations produced according to the method. Rodriguez (2,151,409) teaches human anti-Rho (D) immunoglobulin in aqueous solution in combination with a stabilizing system against molecular addition.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is (703) 305-0487. The examiner can normally be reached on Monday through Thursday from 6:30am to 4:00pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Ja-Na Hines

May 3, 2001

JENNIFER E. GRASER
PRIMARY EXAMINER